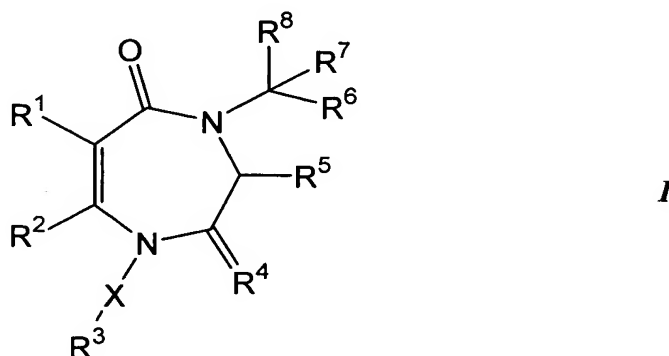


SUBSTITUTED 1,4-DIAZEPINES AND USES THEREOF

ABSTRACT

The present invention is directed to novel 1,4-diazepines, pharmaceutical compositions thereof, and the use thereof as inhibitors of HDM2-p53 interactions. Compounds have Formula *I*:



or a solvate, hydrate or pharmaceutically acceptable salt thereof; wherein:

R^1 , R^2 , R^9 , R^{10} , R^a , R^d and M are defined herein;

X is a bivalent radical of: an alkane, a cycloalkane, an optionally-substituted arene, an optionally-substituted heteroarene, an optionally-substituted arylalkane or an optionally-substituted heteroarylalkane; and

R^3 is $-\text{CO}_2R^d$, $-\text{CO}_2M$, $-\text{OH}$, $-\text{NHR}^d$, $-\text{SO}_2R^d$, $-\text{NHCONHR}^d$, optionally-substituted amidino or optionally-substituted guanidino;

or R^3-X- is hydrogen or an electron pair;

R^4 is oxygen or $-\text{NR}^9R^{10}$;

R^5 is cycloalkyl, aryl, heteroaryl, cycloalkylalkyl, aralkyl, heteroarylalkyl, or a saturated or partially unsaturated heterocycle, each of which is optionally substituted; and

R^6 , R^7 and R^8 are independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, a saturated or partially unsaturated heterocycle, cycloalkylalkyl, aralkyl or heteroarylalkyl, each of which is optionally substituted; or R^6 and

R^7 , together with the carbon atom to which they are attached form a 3- to 7-membered carbocyclic ring optionally substituted 1 to 3 times with R^a .